Attachment B: Literature Review

Author / Title / Journal / Year	Type of Study	Outcomes Studied	Patient Characteristics	Results	HCFA Comments
Caldwell J, Gendreau RM, and Furst D / A pilot study using a staph protein A column (Prosorba) to treat refractory rheumatoid arthritis / The Journal Of Rheumatology / 1999	Prospective Historical controls	Clinical evaluations of RA activity, defined by Paulus criteria Conducted at enrollment, and monthly throughout treatment. Also at 2,4,8,and 12 weeks after last treatment.[4 wks after treatment was the primary endpoint]	15 patients [11 women] with RA who had failed to respond to 2 ore more DMAR Washed out for 1-3 months Duration of study 6 months Underwent treatment once a week for 12 weeks Pts receiving no other form of treatment during this time period. 14/15 pts received all 12 treatments. 1 patients received only 10 treatments.	Base on Paulus 50% criteria, 9/15 pts improved at 4th month. 10/15 were responders by week 20. Adverse events 2.47 per treatment	Open label trial. Good trial design for the purpose of the study-preliminary assessment of the safety and effectiveness of a staph protein A column in the treatment of patients with RA refractory to multiple DMARD therapy. Adverse events fairly mild and minimal, although even patient experienced at least one adverse event. Of note, no patients withdrew secondary to side effects. Mechanism of effect unknown. Slight decrease in IGG noted at one month but no changes in IgA, IgG, or IgM. No change in complement levels, C3, C4, or RF titers.

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Felson DT, LaValley MP, Baldassare AR, Block JA, et al / The Prosorba column for treatment of refractory rheumatoid arthritis / Arthritis and Rheumatism / 1999	Prospective Randomized Placebo-controlled Double-blind Multicenter	Improvement on ACR core set measures: HAQ scale Physician/Patient global assessment Patient pain score CRP level Tender joint count Swollen joint count	91 randomized patients 47 patients in Prosorba arm 44 pts in sham-treated arm 78% female 92% RF positive. Pts had to fail to respond to methotrexate or at least 2 other drugs.Other criteria: >20 tender joints, >10 swollen joints, patient pan score of at least 5 on a 0-10VAS, CRP level of at least 1.25times upper limit of normal. Avg duration of RA 15.5 years (1.7-50.6 yrs) Pts in sham had disease slightly longer than Prosorba group. Failed 4.2 second-line drug treatments prior to entry. Pts received one treatment a week for 12 weeks. Efficacy evaluated 7-8 weeks after treatment ended. Responders defined as showing improvement according to ACR response criteria	DSMB stopped trial early due to successful outcomes. Pts in Prosorba arm, 31.9% experienced improvement vs 11.4% of patients in sham-treated arm (p=.019) [drop out rates: Prosorba 14/47 control 11/44]	Well-designed study. DMSB independent-set criteria established a priori concerning whether trial could be stopped. Wash out period Intention to treat analysis Strict eligibility criteria Power calculation based on an estimated response difference of 20% between Prosorba and sham groups. For this patient population, this appears clinically relevant. Study was being conducted at the same time trials for Enbrel were being conducted. Pts entered into study had not yet tried anti-TNF drugs. Mechanism of effect is unknown. Given intensiveness of treatment, dropout rates are not unreasonable. Avg duration of disease quite widespread. Using logistic regression, authors should no difference in effect based on duration of disease. Side effects included short-term flare in joint pain, and swelling.

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Wiesenhutter CW, Irish BL, and Bertram JH / Treatment of patients with refractory rheumatoid arthritis with extracorporeal protein A Immunoadsorption columns: a pilot trial / The Journal of Rheumatology / 1994	Prospective Case series	67 joints tenderness 64 joints examined for swelling morning stiffness Physician/patient's assessment VAS Grip strength 50' walking time	16 patients asked to participate, 2 declined and 2 who initially agreed subsequently were excluded. 11 patients enrolled with refractory arthritis Pts failed an average of 4.8 DMARD, with mean duration of disease 12.4 yrs No pts previously treated with apharesis. 9 patients received 15 treatments over a 12 week period, 1 patient received 15 treatments over a 15 week period, and 1 patient received 12 treatments over a 9 week period. Duration of trial 24 weeks	9 patients met > 50% criteria at week 13, 4 patients met > 50% and 2 pts met > 20% at week 24. 8 responders continued for 24 weeks without change in arthritic medications, and 2 met ACR criteria for clinical remission at weeks 12 and 28, and remained in remission for > 5 months.	Meant to be a preliminary trial to test whether this therapy is well tolerated and effective in treatment of refractory RA. Pts came from one practice, a single rheumatology private practice in northern Idaho. Concomitant drug therapy was not standardized. 4 pts became symptomatically anemic.